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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/837,491 | 04/18/2001 | Ashit K. Ganguly | IN0931XK | 7916 |

24265 7590 07/28/2003

SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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| EXAMINER |
|---|
| LEWIS, PATRICK T |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1623 | 7 |

DATE MAILED: 07/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/837,491 | GANGULY ET AL. | |
| | Examiner | Art Unit | |
| | Patrick T. Lewis | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Applicant's Response dated May 9, 2003*

1. In the Response filed May 9, 2003, claims 1 and 3-6 were amended. Applicant presented arguments directed to the rejection of claims 1-17 under 35 U.S.C. 112, second paragraph. Claims 1-17 are pending. An action on the merits of claims 1-17 is contained herein below.

2. The amendment dated May 9, 2003 is improper. Applicant has not clearly pointed out what text has been added and/or deleted from the amended claims. Applicant has inserted new text (underlined) but has failed to delete corresponding text. Additionally, no clean copy of the amended claims is presented.

3. The objection to the disclosure is maintained for the reasons of record as set forth in the Office Action dated December 13, 2002.

4. The provisional rejection of claims 1-5 and 15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 25; 2 and 30; 3 and 31; 4 and 32; 13; and 4, respectively, of copending Application No. 09/837,609 ('609) is maintained for the reasons of record as set forth in the Office Action dated December 13, 2002.

5. The rejection of claims 1-5 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 13, 15, 16, and 28 of U.S. Patent No. 6,277,830 B1 is maintained for the reasons of record as set forth in the Office Action dated December 13, 2002.

6. The objection to claims 1, 3, and 13 is maintained for the reasons of record as set forth in the Office Action dated December 13, 2002. The amendment dated May 9, 2003 has rendered the objection to claim 5 moot.

7. The rejection of claims 1-17 under 35 U.S.C § 112, second paragraph, is maintained. Applicant should note that claims 1-17 have been rejected for several reasons. Applicant's amendment has addressed several of the items cited as the basis for the rejection of claims 1-17 under 35 U.S.C § 112, second paragraph; however, applicant's amendment and arguments are not sufficient to overcome the rejection in toto. For the sake of clarity, the examiner will set forth the basis for which claims 1-17 are currently rejected under the section ***Claim Rejections - 35 USC § 112*** herein below.

***Objections/Rejections Set For the in Office Action dated December 13, 2002***

8. The disclosure is objected to because of the following informalities:

Each sentence/paragraph should end in appropriate punctuation including sentences/paragraphs wherein a figure, table, or scheme is incorporated. Items in a list should be separated by appropriate punctuation. See pages 1, 8, 9, 11, 12, 13, 14, 15, 16, 17, 22, 25, 26, 31, 32, 36, 39, 40, 41, 42, 48, 49, 54, 55, 56, 57, 60, 61, and 62. Atoms/bonds in chemical structural formulae should be clearly indicated. See pages 22, 27 (brackets), and 36.

Appropriate correction is required.

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1-5 and 15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 25; 2 and 30; 3 and 31; 4 and 32; 13; and 4, respectively of copending Application No. 09/837,609 ('609). Although the conflicting claims are not identical, they are not patentably distinct from each.

Claim 1 is drawn to a compound represented by formula (II) wherein at lease one of $R^{2'}$, $R^{3'}$ or $R^{5'}$ is H, $R^{20}$-$(W)_x$-CO-, $R^{20}$-$(W)_x$-CS- or $R^{20}$-$(W)_x$-PO(OH)- and wherein at least one of $R^{2'}$, $R^{3'}$ or $R^{5}$ is not H or a pharmaceutically acceptable salt thereof. Claim 2 is drawn to a pharmaceutical composition of a compound of claim 1 together with a pharmaceutically acceptable carrier.

The '609 application differs from the instantly claimed invention in that '609 is drawn to a compound (pharmaceutical composition) wherein at least one of $R^{2'}$, $R^{3'}$ or $R^{5'}$ is a straight or branched chain polyalkene oxide polymer conjugate. The description of variables $R^{2'}$, $R^{3'}$ and $R^{5'}$ in the instantly claimed invention is unclear, ambiguous, and confusing as each of the variables have not been clearly defined. Indeed, the claims of

the '609 application and the instant invention overlap substantially, for example, when $R^{2'}$ ('609) is a straight or branched chain polyalkene oxide polymer conjugate [not H] and $R^{3'}$ ('609) is H, and to issue a patent to the claims of the instant application could result issuing two patents for the same invention.

Claim 3 is drawn to a method of using a compound represented by formula (II) of claim 1 for treating a susceptible viral infection, wherein the method comprises a therapeutically effective amount of a ribavirin derivative of formula (II) or a pharmaceutically acceptable salt thereof. Claim 4 is drawn to a method of using a compound represented by formula (II) of claim 1 for treating a susceptible viral infection, wherein the method comprises a therapeutically effective amount of a ribavirin derivative of formula (II) or a pharmaceutically acceptable salt thereof and a therapeutically effective amount of an interferon alpha. Claim 5 depends from claim 4 and limits the interferon-alpha to interferon alpha-2a, interferon alpha-2b, a consensus interferon, a purified interferon alpha product or a pegylated interferon-alpha-2a, pegylated interferon-alpha-2b, or pegylated consensus interferon.

The '609 application differs from the instantly claimed invention in that '609 is drawn to a method of treating a patient having chronic hepatitis C infection comprising administering a therapeutically effective amount of a ribavirin derivative wherein at least one of $R^{2'}$, $R^{3'}$ or $R^{5'}$ is a straight or branched chain polyalkene oxide polymer conjugate. The description of variables $R^{2'}$, $R^{3'}$ and $R^{5'}$ in the instantly claimed invention is unclear, ambiguous, and confusing as each of the variables have not been clearly defined. Indeed, the claims of the '609 application and the instant invention overlap substantially,

for example, when $R^{2'}$ ('609) is a straight or branched chain polyalkene oxide polymer conjugate [not H] and $R^{3'}$ ('609) is H, and to issue a patent to the claims of the instant application could result issuing two patents for the same invention.

Claim 15 is drawn to a method of treating patients having chronic hepatitis C infection comprising administering a therapeutically effective amount of ribavirin derivative of formula (I) and a therapeutically effective amount of an interferon alpha for a time period sufficient to eradicate detectable HCV-RNA at the end of said period of administering and to have no detectable HCV-RNA for at least 24 weeks after the end of said period of administrating, and wherein at lease one of $R^{2'}$, $R^{3'}$ or $R^{5'}$ is H, $R^{20}$-$(W)_x$-CO-, $R^{20}$-$(W)_x$-CS- or $R^{20}$-$(W)_x$-PO(OH)- and wherein at least one of $R^{2'}$, $R^{3'}$ or $R^5$ is not H or a pharmaceutically acceptable salt thereof.

The '609 application differs from the instantly claimed invention in that '609 is drawn to a method of treating patients having chronic hepatitis C infection comprising administering a therapeutically effective amount of ribavirin derivative of formula (I) and a therapeutically effective amount of an interferon alpha wherein at least one of $R^{2'}$, $R^{3'}$ or $R^{5'}$ is a straight or branched chain polyalkene oxide polymer conjugate. The description of variables $R^{2'}$, $R^{3'}$ and $R^{5'}$ in the instantly claimed invention is unclear, ambiguous, and confusing as each of the variables have not been clearly defined. Indeed, the claims of the '609 application and the instant invention overlap substantially, for example, when $R^{2'}$ ('609) is a straight or branched chain polyalkene oxide polymer conjugate [not H] and $R^{3'}$ ('609) is H, and to issue a patent to the claims of the instant application could result issuing two patents for the same invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Claims 1-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 13, 15, 16, and 28 of U.S. Patent No. 6,277,830 B1. Although the conflicting claims are not identical, they are not patentably distinct from each.

Claims 1-5 are drawn to compounds/methods as described herein above.

The '830 patent differs from the instantly claimed invention in that '830 is drawn to a compound (pharmaceutical composition) or method of treatment wherein $R^{2'}$ is H, $R^{3'}$ is H, and $R^{5'}$ is $CH_3CH(NH_2)$-CO-, $CH_3CH_2(CH_3)CHCH(NH_2)$-CO- or $H_2N(CH_2)_4CH(NH_2)$-CO-. The description of variables $R^{2'}$, $R^{3'}$ and $R^{5'}$ in the instantly claimed invention is unclear, ambiguous, and confusing as each of the variables have not been clearly defined. Indeed, the claims of the '830 patent and the instant invention overlap substantially, and to issue a patent to the claims of the instant application would be to extend the patent term for the subject matter patented in '520.

12. Claims 1, 3, 5, and 13 are objected to because of the following informalities: In claim 1, line 13, a space between "," and "$R^{3'}$". Claim 3 contains two periods. A conjunction is missing in claim 5. In claim 13, the brackets should be replaced by parenthesis in the term "$[CH_3]_2N$". Appropriate correction is required.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, lines 11-14, variables $R^{2'}$, $R^{3'}$ and $R^{5'}$ are unclear, ambiguous, and confusing as each of the variables have not been clearly defined. For example, when $R^{2'}$ is $R^{20}$-$(W)_x$-CO- (not H) the conditions of claim 1 are met; however, $R^{3'}$ and $R^{5'}$ are not defined. The variable "Y" has not been defined (page 97, line 1). The alternate manner in which variables are claimed is unclear, ambiguous, and confusing (page 97, lines 2-3). All claims wherein the variables have not been clearly are indefinite.

Applicant's use of the term "heterocyclic" is unclear as heterocyclic compounds incorporate a heteroatom. Applicant's description of moieties incorporated by the term "heterocyclic" (pages 21-22 of instant specification) is inconsistent with the accepted meaning as a heteroatom may not be part of the ring. The incorporation of said term renders all claims in which they appear indefinite.

Claims 3-5 provide for the use of a compound of formula (II), but, since the claim does not set forth any positive, active steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 6-7 recite the limitation "interferon-alpha administered" in line 1. There is insufficient antecedent basis for this limitation in the claim. The abbreviations "TIW" and

"QOD" have not been defined. The incorporation of said abbreviations renders all claims in which they appear indefinite.

In claims 12-14, it is unclear how moieties representing $R^{5'}$ are attached to the structural core.

In claims 12 and 15, the alternate manner in which variables are claimed is unclear, ambiguous, and confusing (page 99, lines 2-4; page 100, lines 7-8 and 18-20).

In claim 15, the abbreviation "HCV-RNA" has not been defined. The incorporation of said abbreviation renders all claims in which it appears indefinite.

***Response to Arguments***

15. Applicant's arguments filed May 9, 2003 have been fully considered but they are not persuasive.

Applicant's arguments are directed to claim rejections under 35 U.S.C. 112, second paragraph. Applicant argues that: 1) one skilled in the art would readily ascertain the meaning of variable $R^{2'}$, $R^{3'}$ and $R^{5'}$; and 2) one skilled in the art would be apprised of the scope of the term "heterocyclic" in view of the definition and examples provided.

Regarding applicant's argument that one skilled in the art would readily ascertain the meaning of variable $R^{2'}$, $R^{3'}$ and $R^{5'}$, the examiner respectfully disagrees. Variables $R^{2'}$, $R^{3'}$ and $R^{5'}$ are not properly defined. Only one variable is necessarily defined. For example when $R^{2'}$ is $R^{20}$-$(W)_x$-CO- the limitations set forth is claim 1 are met (at lease one of $R^{2'}$, $R^{3'}$ or $R^{5'}$ is H, $R^{20}$-$(W)_x$-CO-, $R^{20}$-$(W)_x$-CS- or $R^{20}$-$(W)_x$-PO(OH)- and wherein

at least one of $R^{2'}$, $R^{3'}$ or $R^5$ is not H). While it is true that $R^{3'}$ **could be** H, and $R^{5'}$ **could be** the same as $R^{2'}$, no such requirement is set forth by the claim.

Regarding applicant's argument that one skilled in the art would be apprised of the scope of the term "heterocyclic" in view of the definition and examples provided, the examiner respectfully disagrees. Applicant has defined the term "heterocyclic" on pages 21-22 of the specification. When variables **I** and **J** are $-CR^{60}$ and $-CHR^{60}$, respectively, the cyclic structural formula applicant asserts as "heterocyclic" does not conform to the conventional definition of "heterocyclic" as no heteroatom is present. No proviso is provided indicating that variables **I** and **J** cannot be $-CR^{60}$ and $-CHR^{60}$, respectively, in the cyclic structure.

### *Claim Rejections - 35 USC § 112*

16. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

17. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The variables $R^{2'}$, $R^{3'}$ and $R^{5'}$ are unclear, ambiguous, and confusing as each of the variables have not been clearly defined. Applicant has failed to set forth clear and distinct definitions of the variables. The phrase "wherein at least one of $R^{2'}$, $R^{3'}$ and $R^{5'}$ is" only defines a single variable. One of ordinary skill in the art would not be apprised of the metes and bounds of the instantly claimed invention as the two remaining

variables have not been distinctly claimed and particularly pointed out. All claims reading upon variables $R^{2'}$, $R^{3'}$ or $R^{5'}$ wherein each variable is not distinctly claimed are deemed indefinite.

The term "heterocyclic" as defined by applicant does not conform to the conventional art-recognized definition of compounds of this class. Applicant has defined the term "heterocyclic" on pages 21-22 of the specification. When variables **I** and **J** are $-CR^{60}$ and $-CHR^{60}$, respectively, the cyclic structural formula applicant asserts as "heterocyclic" does not conform to the conventional definition of "heterocyclic" as no heteroatom is present. No proviso is provided indicating that variables **I** and **J** cannot be $-CR^{60}$ and $-CHR^{60}$, respectively, in a singular cyclic structure.

***Conclusion***

18. Claims 1-17 are pending. Claims 1-17 are rejected. No claims are allowed.

19. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Contacts***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 703-305-4043. The examiner can normally be reached on M-F 8:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Patrick T. Lewis, PhD
Examiner
Art Unit 1623

James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

ptl
July 23, 2003